supplement. Trends Pharmacol. Sci., Elsevier, pp. 65-68 (1997) **[and http://www-biology.ucsd.edu/~msaier/transport/titlepage2.html]**.

Paragraph 2: Ion channels are generally classified by structure and the type of mode of action. For example, extracellular ligand gated channels (ELGs) are comprised of five polypeptide subunits, with each subunit having 4 membrane spanning domains, and are activated by the binding of an extracellular ligand to the channel. In addition, channels are sometimes classified by the ion type that is transported, for example, chlorine channels, potassium channels, etc. There may be many classes of channels for transporting a single type of ion (a detailed review of channel types can be found at Alexander, S.P.H. and J.A. Peters (1997). Receptor and ion channel nomenclature supplement. Trends Pharmacol. Sci., Elsevier, pp. 65-68 **[and http://www-biology.ucsd.edu/~msaier/transport/toc.html].**

Paragraph 3: The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm. (Computational Molecular Biology, Lesk, A.M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at http://www.gcg.com), using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (Devereux, J., et al., Nucleic Acids Res. 12(1):387 (1984)) **[(available at http://www.gcg.com)]**, using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Myers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program

(version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

Paragraph 4:

DESCRIPTION OF THE FIGURE SHEETS

[FIGURE 1] **Figures 1A-1B** provides the nucleotide sequence of a cDNA molecule that encodes the transporter protein of the present invention. (SEQ ID NO:1) In addition structure and functional information is provided, such as ATG start, stop and tissue distribution, where available, that allows one to readily determine specific uses of inventions based on this molecular sequence. Experimental data as provided in Figure 1 indicates expression in humans in embryos (particularly in the head), hepatocellular carcinomas, liver (including non-cancerous liver tissue), fetal liver/spleen, and a mixed brain/heart/kidney/lung/spleen/testis/leukocyte sample.

[FIGURE 2] **Figures 2A-2D** provides the predicted amino acid sequence of the transporter of the present invention. (SEQ ID NO:2) In addition structure and functional information such as protein family, function, and modification sites is provided where available, allowing one to readily determine specific uses of inventions based on this molecular sequence.

[FIGURE 3] **Figures 3A-3X** provides genomic sequences that span the gene encoding the transporter protein of the present invention. (SEQ ID NO:3) In addition structure and functional information, such as intron/exon structure, promoter location, etc., is provided where available, allowing one to readily determine specific uses of inventions based on this molecular sequence. As illustrated in Figure 3, SNPs were identified at 55 different nucleotide positions.

Marked-Up Copy of Amended Claim

4. (Amended) An isolated nucleic acid molecule consisting of a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence that encodes a protein comprising the amino acid sequence of SEQ ID NO: 2;

(b) a nucleotide sequence [nucleic acid molecule] consisting of [the nucleic acid sequence of] SEQ ID NO 1;

(c) a nucleotide sequence that is completely complementary to a nucleotide sequence of (a)-(b).

24. (Amended) A process for producing a polypeptide comprising culturing the host cell of claim 9 under conditions sufficient for the production of said polypeptide from a nucleic acid molecule that encodes said polypeptide, and recovering said polypeptide from the host cell culture.

25. (Amended) An isolated polynucleotide consisting of a nucleotide sequence set forth in SEQ ID NO: [2]1 .

27. (Amended) A vector according to claim 8, wherein said isolated nucleic acid molecule is inserted into said vector in proper orientation and correct reading frame such that the protein of SEQ ID NO: [4] 2 may be expressed by a cell transformed with said vector.

28. (Amended) A vector according to claim 27 [28], wherein said isolated nucleic acid molecule is operatively linked to a promoter sequence.

REMARKS

Sequence compliance objection:

The Examiner objected the sequences disclosed in Figure 2 because the required reference to the relevant sequence identifiers are not accompanied other than SEQ ID Nos: 4 and 5. Applicants hereby complied with the Sequence rule set forth under 37 CFR 1.821(a)(1) and (a)(2), by labeling all the sequences in the Figures.

Objection to the Description of Drawings:

Description of the drawing has been changed. Figure 1 is referred as Figures 1A-1B. Figure 2 is referred as Figures 2A-2D. Figure 3 is referred as Figures 3A-3X.

Objection to the Disclosure:

The examiner objected to the disclosure because it contains an embedded hyperlink and/or other form of browser-executable code (page 2, 1st paragraph, page 5, lines 4-5 and page 21, lines 19-24). Applicants have deleted the URL's from the specification, as indicated above by the replacement paragraphs.

Rejection under 35 USC §101 and §112, 1st paragraph:

At page 5 of the Office Action, the Examiner has rejected claims 4, 8, 9, and 24-28 under 35 U.S.C.§101 and §112, 1st paragraph. In summary, the Examiner has stated that the claimed isolated nucleic acid molecules lack a specific and substantial utility or a well-established utility and, consequently, one skilled in the art would not know how to use the claimed invention.

Applicants respectfully traverse this rejection based on the following remarks.

In contrast to the Examiner's assertions, the claimed isolated nucleic acid molecules, such as SEQ ID NOS: 1 and 3, that encode a specified amino acid sequence, SEQ ID NO: 2, and methods of making and using such nucleic acid molecules have several uses that meet the requirements of 35 U.S.C.§101 and the first paragraph of 35 U.S.C.§112. These, as well as the accepted state of the art view that such molecules have uses within the commercial marketplace in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets, establishes the utility of the claimed invention.

The utility requirement of a claimed invention requires that an invention must have a specific, substantial and credible utility. These requirements are defined in broad terms in cases such as *Brenner v. Manson,* 148 USPQ 689 (S. Ct. 1966) and the recently adopted Utility Guidelines from the USPTO.

The Examiner stated that the present invention failed to disclose any properties of the present invention, SEQ ID NO: 2 that associated with any disease state. However, such a requirement substantially conflicts with the decision made by the CCPA.

The CCPA in *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980), clearly accepted a showing of less than a specific therapeutic use of a claimed chemical compound as satisfying the utility requirement.

> *The CCPA held that where a claim does not provide evidence of pharmacological activity of a claimed compound, although it does not establish a specific therapeutic use, manifests a practical utility because knowledge of pharmacological activity is beneficial to the public in that it makes faster and easier for medical researchers to combat illnesses. Nelson v. Bowler, 206 USPQ 881 (CCPA 1980).*

The notion that a recognized valuable addition to even entry points of the drug discovery cycle advances the art sufficient to establish a "usefulness" of a claimed invention should not be ignored. Similar to the *Nelson* case, the present invention, which is drawn to isolated nucleic acid molecules that encode a transporter protein (SEQ ID NO: 2), has useful value in the drug discovery process even though the molecule may not be associated with a specific treatment and/or diagnosis of a particular disease. According to *Nelson*, the present invention provides sufficient knowledge and information that is beneficial to the public, and provides sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/or diagnostics. It is well recognized that transporters are the most important targets for drug action (pages 1-14 of the specification). The public disclosure of a new member of this family through the patenting process clearly advances the art and augments the capabilities of biomedical researchers to combat illnesses.

The utility rejection raised by the Examiner also conflicts with the case *Juicy Whip v. Orange Bang* (Fed. Cir. 1999). *Juicy Whip* held that, in order to violate the utility requirement, an invention must be "totally incapable of achieving a useful result." The polypeptides and

encoding nucleic acid molecules of the present invention are well known in the art to be valuable drug targets and therefore have readily apparent commercial utilities, such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers, etc. In addition to the uses disclosed in the specification and discussed herein for the polynucleotides of the present invention, other utilities are readily apparent to one of ordinary skill in the art based on the observed tissue specific expression patterns. Specifically, the proteins/nucleic acid molecules of the present invention are expressed in whole embryo, hepatocellular carcinoma, non-cancerous liver, fetal liver spleen, and liver. Thus, for example, the proteins/nucleic acids of the present invention are commercially useful for developing therapeutic agents for treating diseases affecting these tissues. Therefore, the present invention is not "totally incapable of achieving a useful result." Instead, it is useful.

The specification and figures show that the protein of the present invention has functional domain of transporter (see Figure 2, for example, the Prosite and Hmm results). The disclosure of the function of the transporter is sufficient. Such a function is quite specific for transporter proteins and differentiates them from other proteins. As such, this function is specific enough to define a use for novel transporter proteins and transporter-encoding nucleic acid molecules in the drug discovery process.

Novel transporter proteins/nucleic acids are commercially useful for developing therapeutics/diagnostics for these and other pathologies. Thus, there is overwhelming evidence in the art to support the utility of novel transporter proteins and encoding nucleic acid molecules, particularly those related to amino acid transport system A (ATA) family. Not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses. These uses are quite specific for the transporter family of proteins, even though each member may play a somewhat different role in cellular responses and pathologies. Even though each member may have a somewhat different role in biology and disease, each is a specific composition of matter having substantial, specific and credible uses that the vast majority of other isolated nucleic acid molecules do not possess.

By placing a new member of the transporter protein family into the public domain through the patenting process, the present invention is not only a clear advancement over the prior art (a newly discovered protein/gene) but also enables significant advancement in medicine and further

discovery. The Utility requirement cannot be used to contradict the reasons for the patent system, to encourage early disclosures of inventions so that others can benefit from, improve upon, and further develop such inventions. This is particularly important in medicine, wherein early disclosure of key inventions (such as new transporter proteins and encoding nucleic acid molecules) is needed to facilitate the early development of new therapies and diagnostics to treat illnesses.

The grant of a patent to the claimed isolated nucleic acid molecule and the resultant disclosure of the nucleic acid and protein sequences to the public will certainly shorten the process for medical researchers to discover other novel uses for the present transporter-encoding nucleic acids. One example disclosed in the specification is that the present nucleic acid molecules can be used to produce protein targets for identifying agents that bind to the protein targets and modulate protein function. Such agents can be used to precisely determine which biological and pathological processes the protein is involved in. Furthermore, such agents that bind to a protein target and modulate cell signaling may subsequently be developed and refined for use in mammalian therapeutic applications. All of this later discovery and refinement will be done using the presently claimed material. These uses are clearly commercial and substantial uses that are specific for a very limited number of proteins/nucleic acid molecules.

In addition to serving as targets for developing molecular probes and therapeutic agents, the disclosed uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediates, particularly in biological assays, is sufficient to satisfy the requirements of 35 USC §101 and §112. The claimed invention is directed to nucleic acid sequences that encode a transporter protein with a specified amino acid sequence (SEQ ID NO: 2), such as SEQ ID NOS: 1 and 3. Exemplary uses of the nucleic acid sequences are clearly recited in the specification on, for example, pages 43-63. Among the examples, the nucleic acid molecules are useful as hybridization probes for messenger RNA molecules, transcript/cDNA molecules, genomic DNA, and variants thereof. An expression vector comprising the nucleic acid sequences can be made that expresses the transporter protein. Such uses are specific for the claimed nucleic acid molecules, and the products of such uses will be clearly different (and hence specific for the claimed molecules) than what would be produced using a different nucleic acid molecule for the same purpose.

In view of law and fact, the utility standard interpreted by the USPTO guidelines is too high. The disclosure of activity of the expressed polynucleotide is not required by any statute or case law interpreting the utility requirement of Section 101, and the enablement requirement of Section 112, first paragraph. The commercial value of a gene that encodes a previously unidentified member of the transporter protein family, members of which are well known in the art to be commercially valuable drug targets, should be sufficient to satisfy the utility requirement.

Rejections under 35 USC §112, 2nd paragraph:

The Examiner rejected claims 24, 25, 27, 28 under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is dependent from claim 4(d), which is directed to a complementary nucleic acid sequence. The examiner stated that it is unclear how one would be able to produce a polypeptide from the complementary sequences, or which of the several, short open reading frames encoded by the complement are intended.

In response, Applicants have amended claim 24 which specifically recited "a nucleic acid molecule that encodes said polypeptide." The said polypeptide is SEQ ID NO: 2.

Rejections to claims 25, 27 and 28 for incorrect SEQ ID NOs and claim dependency are overcome by the amendment shown above.

Applicants believe the amendment and the explanation satisfy the requirement under 112, 2nd paragraph. Therefore, the rejection to claims 24, 25, 27 and 28 should be withdrawn.

Conclusions

Claims 4, 8-9, and 24-28 are currently pending.

In view of the above remarks and amendments, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,

CELERA GENOMICS

Date: June 12, 2003

By: _____

Lin Sun-Hoffman, Ph.D., Reg No. 47,983

Celera Genomics Corporation
45 West Gude Drive, C2-4#21
Rockville, MD 20850
Tel: 240-453-3628
Fax: 240-453-3084